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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,477	03/01/2002	Sean C. Semple	INEX.P-006-2	3225

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EXAMINER	
NGUYEN, DAVE TRONG	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,477	SEMPLE ET AL.	
	Examiner	Art Unit	
	Dave T Nguyen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12 and 14-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 1 and 3 are amended by the amendment filed Feb 3, 2005.

Claims 1, 3-12, and 14-19 are pending for examination.

The first paragraph of the specification is objected because the status of Application No. 09/649,527 needs to be updated to reflect its abandoned status.

The rejection under 35 USC 112, first paragraph is withdrawn because of applicant's claim amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order

for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5-8, 11, 14, and 16-19 remain rejected under 35 USC 103 as being unpatentable over Krieg (US 6,207,646) or Krieg (US 6,429,199) taken with any of Wheeler *et al.* (US Pat No. 5,981,501), MacLachlan (WO 99/397741) or Semple (WO 98/51278).

The examiner's response to applicant's response on pages 5-7:

Applicant asserts that since Krieg(s) does not provide a working example of a lipid-based delivery vehicle and does not teach a fully encapsulated CpG based nucleic acid, the examiner appears to pick and choose among the prior art teachings in order to reconstruct the claimed invention. However, the response is not found persuasive because the fact that Krieg(s) do not provide a working example does not necessarily mean that the examiner has ignored the teachings provided by the totality of the prior art of record, nor is it apparent that one of ordinary skill would not have been motivated to employ a lipid carrier or liposome to enhance the delivery of a CpG based nucleic acid to an individual. Applicant appears to start the rebuttal by focusing solely on the Krieg(s) references rather than assessing the totality of the prior art of record with respect to the combination use of a CpG based oligo encapsulated fully within a lipid particle comprising a cationic lipid. As the examiner has stated previously, the art of making lipid particle comprising a cationic lipid as a carrier in encapsulating a bioactive agent such as DNA is well known in the prior art.

See all of the cited art of record. The main thrust of the claimed invention is a the make and use of a CpG based nucleic acid encapsulated fully within a lipid particle comprising a cationic lipid. As such, the fact that Krieg does teach that a CpG based nucleic acid can be used in combination with and/or encapsulated within a cationic lipid-based lipid, and the fact that the secondary references provide number extensive teachings regarding the advantages of employing lipid particles with mean diameter of 50-200 nm are sufficient to enable one of ordinary skill in the art to arrive at the invention without any selected pick and choose of any particular teaching of any particular prior art. Applicant further asserts on page 6 that since the parent application does not provide any written support for the claimed invention as pending, then the same standard must be applied to the totality of the prior art of record. In other words, applicant again appear to argue the secondary references individually without any regard of the totality of the teachings provided by all of the combined cited references. First, the written support and/or concept of employing a a CpG based nucleic acid that can be used in combination with and/or encapsulated within a cationic lipid-based lipid are clearly taught in the primary references. Next, the issue is then whether the concept of making lipid articles especially those having mean diameter of less than 200 nm is well taught in the prior art, and whether such lipid particles have been to enhance the delivery of nucleic acid molecules to cells. Those two issues are taught and disclosed extensively in the secondary references. The fact that the secondary references are also directed to the making and use of gene therapy vectors encapsulated within lipid particles do not constitute a teaching away

element as suggested by applicants. Applicant also appears to suggest the teaching away element in the Dow reference or post filing arts, however, such references are not available in the prior art at the time of filing. And even if they are, such teachings do not in any way teach that encapsulated lipid particles would not render the DNA/lipid encapsulated particles not more immunostimulatory than the DNA administered alone. As such, the examiner maintains that reliance on applicant's disclosure and/or data are not in any way a part of the stated rejection.

Claims 1, 3, 5-12, 14, 16-19 also remain rejected under 35 USC 103(a) as being unpatentable over Krieg (US 6,207,646) or Krieg (US 6,429,199) taken with any of Wheeler *et al.* (US Pat No. 5,981,501), MacLachlan (WO 99/397741) or Semple (WO 98/51278), and further in view of Meers.

The citation of Tam in the previous rejection is a typographical error and thus, is correct in this stated rejection. The body of the previous rejection is maintained fully in this stated rejection.

Applicant 's assertion (page 8) is essential the same as set forth above, and thus, is also not persuasive because of the reasons as set forth in the preceding paragraphs.

The examiner further maintains that the additional citations such as McEver and Boulikas are simply to indicate that the concept and/or advantages of encapsulated nucleic acid/lipid particles are well-known, and are not cited to indicate that the claimed invention is anticipatory. Given that oligonucleotide containing a

CpG is a nucleic acid, that Krieg(s) clearly teach that oligonucleotide can be encapsulated within a lipid particle, and that lipid particles with mean diameter of less than 200 nm were routinely made for use in enhancing the delivery and stability of a nucleic acid when encapsulated within which and when administered to an *in vivo* environment, one of ordinary skill in the art would necessarily have been motivated to employ a lipid particle of the cited prior art as set forth in the stated rejection in encapsulating and delivering a CpG based oligonucleotide of the primary references *in vivo.*

In summary, the first issue is whether or not the prior art of record teaches an encapsulating lipid carrier. The stated rejections of record do provide evidentiary support to demonstrate that the concept of making an encapsulating lipid carrier as an a nucleic acid delivery complex is routine and conventional in the prior art of record. The second issue is whether or not a skilled artisan would have been motivated to employ the DODMA and DODAP/PEG-lipid/DOPE of Wheeler or Meers as an encapsulating lipid delivery vector. Thus, the stated rejection of record does teach, suggest, and provide a motivation for a skilled artisan to employ the DODMA and DODAP/PEG-lipid/DOPE of Wheeler or Meers as an encapsulating lipid delivery vector to deliver the oligonucleotide of Krieg.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Ram Shukla*, may be reached at **571-272-0735.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Central Fax number, which is **571-273-8300**.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

DAVE TRONG NGUYEN
PRIMARY EXAMINER